August 19, 2002

Connie L. Deford
Global Environment, Health and Safety Manager
The Dow Chemical Company
2020 Dow Center
Midland, MI 48674

Dear Ms. Deford:

The Office of Pollution and Toxics is transmitting EPA's comments on the robust summaries and test plan for Ethyl Monochloroacetate posted on the ChemRTK HPV Challenge Program Web site on January 24, 2002. I commend The Dow Chemical Company for its commitment to the HPV Challenge Program.

EPA reviews test plans and robust summaries to determine whether the reported data and test plans will provide the data necessary to adequately characterize each SIDS endpoint. On its Challenge Web site, EPA has provided guidance for determining the adequacy of data and preparing test plans used to prioritize chemicals for further work.

EPA will post this letter and the enclosed Comments on the HPV Challenge Web site within the next few days. As noted in the comments, we ask that The Dow Chemical Company advise the Agency, within 60 days of this posting on the Web site, of any modifications to its submission.

If you have any questions about this response, please contact Richard Hefter, Chief of the HPV Chemicals Branch, at 202-564-7649. Submit questions about the HPV Challenge Program through the HPV Challenge Program Web site "Submit Technical Questions" button or through the TSCA Assistance Information Service (TSCA Hotline) at (202) 554-1404. The TSCA Hotline can also be reached by e-mail at tsca-hotline@epa.gov.

I thank you for your submission and look forward to your continued participation in the HPV Challenge Program.

Sincerely,

-S-

Oscar Hernandez, Director
Risk Assessment Division

Enclosure

cc: W. Sanders
A. Abramson
C. Auer
M. E. Weber

EPA Comments on Chemical RTK Challenge Submission:
Ethyl Monochloroacetate

SUMMARY OF EPA COMMENTS

The Sponsor, The Dow Chemical Company, submitted a test plan and robust summaries to EPA on ethyl monochloroacetate (CAS No. 105-39-5) on December 18, 2001. EPA posted the submission on the Chemical RTK HPV Challenge Web site on January 24, 2002.

EPA has reviewed the submission and has reached the following conclusions:

1. Physiochemical and Environmental Fate Data. The submitter needs to indicate whether the submitted physicochemical data are calculated or measured and make some corrections to the transport and distribution robust summary.

2. Health Effects. (a) The submitter needs to conduct testing for the chromosomal aberration endpoint. (b) The submitter needs to provide additional information to satisfy the requirements for classification of ethyl monochloroacetate as a "closed system intermediate." (c) Data on the developmental toxicity endpoint are needed.

3. Ecological Effects. (a) EPA disagrees with the submitter that no further testing is required for aquatic invertebrates. (b) EPA reserves judgment on the adequacy of the fish toxicity endpoint pending the receipt of missing data elements in the robust summary. (c) EPA agrees with the submitter that testing is required for algae.

EPA requests that the submitter advise the Agency within 60 days of any modifications to this submission.

EPA COMMENTS ON THE ETHYL MONOCHLOROACETATE CHALLENGE SUBMISSION

General Comments

The substance is described as a "closed system intermediate" produced by the submitter at a single facility and used primarily as an intermediate in organic synthesis. The closed system process is described, but no specific information was provided for another company that is an importer of ethyl monochloroacetate.

Test Plan

Physicochemical properties and environmental fate

The submitter did not indicate in the test plan or robust summaries if the physicochemical data provided are calculated or measured (except for octanol/water partition coefficient). Certain measured values should be supplied for these chemicals. In particular, boiling points (decomposition points if appropriate), water solubilities, and vapor pressures should be measured unless precluded by experimental obstacles. The use of estimated values introduces uncertainties that then become magnified in modeling applications.

Fugacity. The sponsor estimated the fugacity of these chemicals using a Level I EQC model. Although EPA had previously recommended the use of EQC Level I, this model is somewhat limited. EPA now recommends a level III analysis, which is more rigorous. The EQC and EPIWIN Level III models are acceptable.

Health Effects (acute toxicity, repeated-dose toxicity, genetic toxicity, and reproductive/developmental toxicity).

Adequate data are available for the acute and genetic (gene mutation) toxicity endpoints for the purposes of the HPV Challenge Program. Data on chloroacetic acid may be used to characterize developmental toxicity, and support other endpoints, if the sponsor can establish that the enzymatic hydrolysis of ethyl monocholoroacetate is sufficiently rapid to infer significant systemic exposure to the former (data on chloroacetic acid where submitted under the OECD SIDS Program).

Genetic Toxicity (in vitro). Chromosomal Aberration. No data are available for this endpoint and no testing is proposed. The submitter needs to conduct testing for the *in vitro* chromosomal aberration endpoint following OECD guidelines.

Repeated-Dose Toxicity. The submitter cites the summary for a carcinogenicity study as addressing this endpoint, but important study details are missing and the summary is partly in German.

Reproductive Toxicity. No data are available for this endpoint and no testing is proposed, based on the submitter's assertion that ethyl monochloroacetate is a "closed system intermediate." As noted above, the submitter should examine the use of data on chloroacetic acid to address this endpoint.

The Guidance for Testing Closed System Intermediates for the Challenge Program http://www.epa.gov/chemrtk/guidocs.htm allows for a reduced testing protocol provided certain criteria are met. The information required to judge a "closed system intermediate" claim must address the following:

I. Site information
   A. Number of sites.
   B. Basis for "closed process" conclusion at each site.
      1) Process description.
      2) Monitoring data showing no detection.
      3) In the absence of monitoring data, the basis for believing that releases do not occur.
   C. Data on "presence in distributed products."
II. Information on transport (mode, volume, controls, etc)
III. A data search showing that the chemical is not present in other end products.

EPA does not believe that the information provided by the submitter is adequate to satisfy the requirements for classification as a "closed system intermediate" eligible for reduced testing in the HPV Challenge Program.

The submitter states that another company imports ethyl monochloroacetate into the U.S. The evidence is inadequate to conclude that all sites in the U.S. manufacture, process and distribute this chemical in a manner consistent with the definition of a "closed system intermediate." According to a published source, major uses of ethyl monochloroacetate are as follows: solvent, organic synthesis, military poison and vat dyestuffs (1).

The submitter states that ethyl monochloroacetate is produced at a single facility in a completely closed system, but neither a description of the process nor a flow diagram is provided. Although the submitter provides workplace monitoring data, information is missing on other chemical releases or wastes generated following manufacture, as well as documentation that the chemical is non-detectable in downstream products. A more complete description of the manufacturing process and transfer of the chemical to storage is needed.

EPA therefore reserves judgment on whether ethyl chloroacetate meets the criteria for a "closed system

intermediate," pending the submission of additional information on the operations of the sponsor as well as those of the importer.

Developmental Toxicity. A developmental toxicity study is not available and is not proposed by the submitter because of low exposure potential and the corrosiveness of the chemical. EPA disagrees and believes that this endpoint should be adrressed by either conducting a developmental screening test (OECD TG 421) or by the use of data on the enzymatic hydrolysis product, chloroacetic acid, if the conversion is sufficiently rapid.

Ecological Effects

EPA reserves judgment on the adequacy of the fish toxicity endpoint. Critical missing data elements need to be provided to the robust summary. The aquatic invertebrate study is inadequate. An unfamiliar test method was used and a detailed description of the test protocol is missing. EPA agrees that an algal toxicity test needs to be conducted.

Specific Comments on Robust Summaries

The submitter needs to indicate the purity of the test substance in Section 1.1 General Substance Information of the IUCLID Data Set.

Environmental Fate

Fugacity. Even though the submitter indicates in the test plan that a level I model was used to calculate transport and distribution (page 5), the robust summary indicates that a level III model was used (page 12/44). However, the reported results are for a level I calculation. The submitter needs to correct this discrepancy.

The input values for vapor pressure (649 Pa or 6.49 hPa) and octanol/water partition coefficient (Log Pow 0.94) in Section 3.3.1 of the robust summary do not match the values reported in Section 2.4 (4.5, 4.8, 8.8,13.3 hPa) and Section 2.5 (Log Pow 1.12 and 1.13). The submitter needs to correct this discrepancy. The submitter also needs to indicate if the input values are calculated or measured. As stated above, the submitter needs to use measured data as inputs into the fugacity model as much as possible. The use of estimated values introduces uncertainties that then become magnified in modeling applications.

Health Effects

Some of the submitted robust summaries are partly in German and partly in English; others have both German and English versions. For example, the genetic toxicity study (reference # 57, 58, 59) is summarized partly in German and partly in English on pages 36 and 37. Carcinogenicity studies (Section 5.7) and Other Relevant Information (Section 5.10) are summarized in German only. The translation of robust summaries into English is the responsibility of the submitter. Submissions under the HPV Challenge Program should always be in English to facilitate review and ensure public access through the ChemRTK Web site.

The submitter needs to remove duplicate entries (reference # 60, 61, 62). Also, reference # 60 has been cited three times, two with same test results and one with different test results. The submitter needs to address this issue. Because of the sparseness typical of many IUCLID records, the submitter should ensure that these summaries include all relevant information from the selected studies.

Acute Toxicity. Six oral, 6 dermal, 2 inhalation, and 1 subcutaneous robust summary were submitted. Only one of these summaries (reference 30, an oral study) contained sufficient information to evaluate the study adequately. Information missing from this robust summary includes: test substance, test substance concentrations, number of animals tested, and test results.

Genetic Toxicity. Although the gene mutation endpoint has been adequately addressed, information missing from the robust summaries includes: test substance, test substance concentrations, cytotoxicity data, solvent, positive control, information on metabolic activation system and experimental protocol details.

Ecotoxicity

Fish. One of the two submitted robust summaries was considered adequate because an accepted method was stated as being followed. However, concentrations tested, statistical tests and confidence intervals, age of fish and how test solutions were prepared were not provided.

Follow-up Activity

EPA requests that the submitter advise the Agency within 60 days of any modifications to this submission.

References

1. Hawley's Condensed Chemical Dictionary. 13th ed. New York, NY: John Wiley & Sons, Inc. 1997, as reported in Hazardous Substances Data Bank. http://toxnet.nlm.nih.gov/